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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/171,081	12/14/1998	SASA KRANJC	22681-0002	7627

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EXAMINER

PRATS, FRANCISCO CHANDLER

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 01/23/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/171,081

Applicant(s)

KRANJC ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on November 5, 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-94 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-94 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

The amendment filed November 5, 2002, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 56-94 have been added.

Claims 36-94 are pending and are examined on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 56-59, 62-65, 67, 69 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Cole et al (U.S. Pat. 4,110,165).

Cole discloses processes of making clavulanic acid wherein the claimed microorganism, *Streptomyces clavuligerus*, is cultivated in a fermentation medium. Note specifically the potassium dihydrogen phosphate concentration of 0.1% in the fermentation disclosed in Example 13 at column 23. Note further that about 55% of the dipotassium hydrogen phosphate in the

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fermentation medium in Example 9, at column 21, is "assimilable" phosphorus, i.e. phosphate, and that therefore the medium in Example 9 contains about 1.10 grams of assimilable phosphorus per liter of medium which is about 0.11% assimilable phosphorus, well within the claimed range concentration. Therefore, in at least Examples 9 and 13, the starting phosphorus concentration is below the claimed amount. Moreover, no phosphorus is added during the fermentation, and the fermentations last for 3-5 days. Thus, the processes disclosed in Examples 9 and 13 necessarily meet the limitation requiring the phosphorus concentration to be allowed to decrease as the fermentation proceeds. Moreover Example 9 uses "Arkasoy," or soy flour as the nitrogen source. See column 20, lines 1 and 2. A holding of anticipation over the cited claims is therefore required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 56-65 and 67-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (U.S. Pat. 4,110,165) in view of Stanbury et al (*Principles of Fermentation Technology*, Pergamon Press, New York, 1984, pages 11-25).

As discussed above, Cole discloses processes of making clavulanic acid wherein the claimed microorganism, *Streptomyces clavuligerus*, is cultivated in a fermentation medium containing the claimed amounts of nutrients, including phosphate.

Cole differs from the claims in that Cole does not explicitly disclose processes wherein the phosphorus concentration is maintained within the ranges recited in claims 60, 61, 77 and 78 at the specific time period of the fermentation. Cole also does not explicitly disclose conducting the fermentations as fed-batch or continuous processes, as recited in claims 71, 74 and its dependents, and 92 and its dependents, such that phosphorus is added during the fermentation. However, Cole clearly discloses that 0.1% is a

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suitable concentration of phosphorus for fermentative production of clavulanic acid. See Example 13. Thus, the artisan of ordinary skill at the time of applicant's invention clearly would have been motivated by Cole's disclosure of the suitability of 0.1% phosphorus to have ensured the presence of that amount of phosphorus, as recited in claims 60, 74 and its dependents and 92 and its dependents, in continuous or fed-batch processes of the type disclosed by Stanbury. Moreover, the determination of suitable amounts of phosphorus, such as the narrower ranges recited in claims 61 and 78, would have been a routine matter of optimization of a result-effective parameter, and therefore obvious under § 103(a). Further still, the use of well-known pH control methods such as the addition of ammonium or sodium hydroxide, recited in claim 93, must further be considered obvious, absent some demonstration of unexpected result coming from this well-known method of pH control.

In sum, the claims are directed to fermentation processes requiring maintenance of phosphorus at a concentration disclosed by the prior art as being suitable in that very fermentation process. Absent some demonstration of an unexpected result coming from the claimed concentrations, a holding of obviousness is required.

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Claims 56-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (U.S. Pat. 4,110,165) in view of Stanbury et al (*Principles of Fermentation Technology*, Pergamon Press, New York, 1984, pages 11-25), as applied above to claims 56-65 and 67-94, and in further view of Lawrence et al (British Patent 1 571 888).

As discussed above, when viewed in light of Stanbury, Cole renders obvious the process recited in claims 56-65 and 67-94. Cole differs from claim 66 in not disclosing the use of ammonium sulfate as the nitrogen source. However, Lawrence clearly discloses that inorganic salts including ammonium and sulfate ions can be used as nutrients in culture media used to produce clavulanic acid from *Streptomyces clavuligerus* by fermentation. See page 2, lines 34-37. Thus, the artisan of ordinary skill, recognizing from Lawrence the suitability of salts including ammonium and sulfate ions as nutrients in culture media used to produce clavulanic acid from *Streptomyces clavuligerus* by fermentation, clearly would have been motivated to have used ammonium sulfate in the fermentation processes of Cole, reasonably expecting from Lawrence that successful production of clavulanic acid would result.

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Claims 56-65 and 67-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (U.S. Pat. 4,110,165) in view of Stanbury et al (*Principles of Fermentation Technology*, Pergamon Press, New York, 1984, pages 11-25), as applied above to claims 56-65 and 67-94, and in further view of Puentes et al (EP 0 182 522 A1).

As discussed above, Cole obviates claims 56-65 and 67-94 when taken in view of Stanbury. With the exception of *Streptomyces clavuligerus*, neither of those references discloses the production of clavulanic acid from all of the microorganisms recited in claims 70 and 85. However, Puentes et al disclose that all of the claimed microorganisms were known at the time of applicant's invention to produce clavulanic acid in known media containing carbon sources, nitrogen sources and inorganic salts. See page 2. Thus, the substitution of any known clavulanic acid-producing species for that disclosed in Cole clearly would have been considered an obvious matter of selecting from known equivalents, the artisan of ordinary skill reasonably expecting from Puentes that the microorganisms disclosed therein would be able to produce clavulanic acid in the fermentation media disclosed by Cole. Thus, absent some unexpected result inhering from the use of the claimed microorganisms, the claims must be considered obvious in this respect.

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Interference

Claims 36-55 are rejected under 35 U.S.C. 135(b) as not being made prior to one year from the date on which U.S. Patent No. 6,100,052 was granted. See *In re McGrew*, 120 F.3d 1236, 1238, 43 USPQ2d 1632,1635 (Fed. Cir. 1997) where the Court held that the application of 35 U.S.C. 135(b) is not limited to *inter partes* interference proceedings, but may be used as a basis for *ex parte* rejections.

Specifically, claims 36-55 recite subject matter clearly overlapping and/or encompassing and/or suggested by the subject matter recited in the patented claims. Note specifically that both sets of claims recite the two-stage maintenance of phosphorus concentration, and that applicant's claims clearly recite ranges for the two stages which are encompassed by the patented claims. Thus, claims 36-55 are clearly directed to "substantially the same subject matter" as stated in 35 U.S.C. § 135(b). Moreover, the first appearance of these claims was September 28, 2001, more than one year after the August 8, 2000, issue date of the '052 patent. Thus, rejection under 35 U.S.C. § 135(b) is clearly required.

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Response to Arguments

All of applicant's argument has been fully considered but is not persuasive of error. With respect to the rejection under 35 U.S.C. § 135(b), the '052 patent issued on August 8, 2000. As of the critical date of August 8, 1999, one year prior to the issuance of the '052 patent, applicant's claims required only that the phosphorus concentration had to be "less than 0.15 w/v during a growth phase of the fermentation and is allowed to decrease after cessation of the growth phase." See claim 1; see also claim 16 presented in the preliminary amendment of December 14, 1998. It was not until September 28, 2001, after the issuance of the '052 patent, that the claims positively recited a limitation with respect to the "starting stage" phosphorus concentration. While applicant may have inherent support in the specification for this "starting stage" phosphorus concentration limitation, and while applicant's "starting stage" concentration appears to directly correspond to the "initial soluble phosphate concentration" recited in claim 1 of the '052 patent, the simple fact remains that applicant did not present this parallel claim structure until September 28, 2001, after the issuance of the '052 patent. Applicant's claims simply did not recite any limitation regarding initial or "starting stage" phosphorus concentration until September 28, 2001, after the issuance of

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the '052 patent. Thus, while the '052 patent cannot be considered prior art to the instant claims, 35 U.S.C. 135(b) precludes applicant from instituting an interference with the '052 patent.

With respect to the fact that certain claims depending from claim 36 contain embodiments not explicitly recited or encompassed by the claims of the '052 patent, the fact remains that these claims depend from a claim which, but for applicant's failure to present an interfering claim in a timely manner, interferes with the claims of the '052 patent. Thus, the patentability of the claims dependent on claim 36 is inextricably tied to the patentability of claim 36. If an interference could be declared, these dependent claims would correspond to the "count," and could not be considered allowable unless the count was considered allowable. Thus, because they correspond to the phantom interference "count," the claims dependent on claim 36 must be included in the rejection under 35 U.S.C. § 135(b).

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS**

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ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned

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are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Francisco C Prats
Primary Examiner
Art Unit 1651

FCP
January 21, 2003